Transplantation of Pluripotent Stem Cell Derived Microglia for the Treatment of Adult-onset Leukoencephalopathy (HDLS/ALSP)

Grant Award Details

Transplantation of Pluripotent Stem Cell Derived Microglia for the Treatment of Adult-onset Leukoencephalopathy (HDLS/ALSP)

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-12130

Project Objective: To develop an hPSC-derived microglial cell therapy candidate for adult-onset leukoencephalopathy (ALSP).

Investigator:

Name:	Mathew Blurton-Jones
Institution:	University of California, Irvine
Type:	PI

Disease Focus: Neurological Disorders

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $214,668

Status: Active

Grant Application Details

Application Title: Transplantation of Pluripotent Stem Cell Derived Microglia for the Treatment of Adult-onset Leukoencephalopathy (HDLS/ALSP)

Public Abstract:

Research Objective

We propose to investigate the transplantation of pluripotent stem cell derived microglia as a potential therapy for the devastating neurological disease; Adult-onset leukoencephalopathy (ALSP/HDLS).

Impact

The most immediately impacted condition will be ALSP. However, further examination of the safety of human microglial transplantation will have broad implications for many neurodegenerative disorders

Major Proposed Activities

- We will differentiate the human embryonic stem cells line ESI-017 into micoglia, the primary immune cell of the brain.
- We will assess the purity of stem cell derived microglia by examining multiple markers for microglia and stem cells. We aim to achieve greater than 99% purity.
- We will utilize single cell RNA sequencing as a sensitive method to determine whether any contaminating pluripotent stem cells remain following microglial differentiation.
- Using specialized mice that develop ALSP pathology and allow human cells to be transplanted, we will engraft human microglia into the brain.
- We will allow mice to age for 3 months and then use a series of tests to examine the impact of micorglial transplantation on motor and cognitive function.
- We will examine the impact of human microglial transplantation on ALSP-associated neuropathologies. We will then report our results and schedule a discussion with the FDA.

Statement of Benefit to California:

Adult-onset leukoencephalopathy (ALSP) is a neurological disease that effects patients during the prime of their lives. Although rare, ALSP represents the clearest example of a 'microgliopathy', a disorder that affects microglia, the immune cell of the brain. As microglial dysfunction is implicated in virtually all neurological disorders, the examination of stem cell-derived microglia to treat ALSP could provide important insight into many of the neurological diseases that affect Californians.

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